

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/012474

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/574 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EP0-Internal, BIOSIS, WPI Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>WO 03/039443 A (DEUTSCHES KREBSFORSCH ;HAERLACH TORSTEN (DE); EILS ROLAND (DE); K) 15 May 2003 (2003-05-15) the whole document in particular Examples 4, 6 and 7 ----- -/--</p>	1-27

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

3 March 2005

Date of mailing of the international search report

09.06.2005

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>SCHOCH CLAUDIA ET AL: "Acute myeloid leukemias with reciprocal rearrangements can be distinguished by specific gene expression profiles"</p> <p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 99, no. 15, 23 July 2002 (2002-07-23), pages 10008-10013, XP002215484 ISSN: 0027-8424 the whole document in particular tables 1 and 2</p>	1-27
Y	<p>KOHLMANN A ET AL: "MOLECULAR CHARACTERIZATION OF ACUTE LEUKEMIAS BY USE OF MICROARRAY TECHNOLOGY"</p> <p>GENES, CHROMOSOMES & CANCER, XX, XX, vol. 37, no. 4, August 2003 (2003-08), pages 396-405, XP008025253 the whole document in particular table 2</p>	1-27
Y	<p>DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2002 (2002-11-16), KOHLMANN ALEXANDER ET AL: "A Gene Expression Study of 59 Acute Myeloid Leukemia (AML) Patients with Recurrent Cytogenetic Abnormalities." XP002269490 Database accession no. PREV200300335805 abstract & BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 1205, 44th Annual Meeting of the American Society of Hematology; Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971</p>	1-27
Y	<p>HAERLACH T ET AL: "The Diagnosis of 14 Specific Subtypes of Leukemia Is Possible Based on Gene Expression Profiles: A Study on 263 Patients with AML, ALL, CML, or CLL"</p> <p>BLOOD, W.B.SAUNDERS COMPAGNY, ORLANDO, FL, US, vol. 100, no. 11, 16 November 2002 (2002-11-16), page 139A, XP002263227 ISSN: 0006-4971 the whole document</p>	1-27
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2001 (2001-11-16), SCHOCH CLAUDIA ET AL: "Specific abnormalities on the genomic level result in a distinct gene expression pattern detected by oligonucleotide microarrays: An analysis of 25 patients with AML M2/t(8;21), AML M3/M3v/t(15;17), and AML M4eo/inv(16)" XP002269491 Database accession no. PREV200200129822 abstract & BLOOD, vol. 98, no. 11 Part 1, 16 November 2001 (2001-11-16), pages 92a-93a, 43rd Annual Meeting of the American Society of Hematology, Part 1;Orlando, Florida, USA; December 07-11, 2001 ISSN: 0006-4971</p>	1-27
Y	<p>----- EP 1 043 676 A (WHITEHEAD BIOMEDICAL INST) 11 October 2000 (2000-10-11) the whole document</p>	1-27
Y	<p>----- GOLUB T R ET AL: "Molecular classification of cancer: Class discovery and class prediction by gene expression monitoring" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 286, no. 5439, 15 October 1999 (1999-10-15), pages 531-537, XP002207658 ISSN: 0036-8075 cited in the application the whole document</p>	1-27
Y	<p>----- DUGAS M ET AL: "A comprehensive leukemia database: integration of cytogenetics, molecular genetics and microarray data with clinical information, cytomorphology and immunophenotyping" LEUKEMIA, MACMILLAN PRESS LTD, US, vol. 15, no. 12, December 2001 (2001-12), pages 1805-1810, XP002263731 ISSN: 0887-6924 the whole document</p> <p>----- -/--</p>	1-27

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DUGAS MARTIN ET AL: "Impact of integrating clinical and genetic information." IN SILICO BIOLOGY, vol. 2, no. 3, 2002, pages 383-391, XP001179418 ISSN: 1386-6338 (ISSN print) the whole document	1-27
A	----- HAN WENLING ET AL: "Identification of eight genes encoding chemokine-like factor superfamily members 1-8 (CKLFSF1-8) by in silico cloning and experimental validation." GENOMICS, vol. 81, no. 6, June 2003 (2003-06), pages 609-617, XP002269492 ISSN: 0888-7543 (ISSN print) the whole document	1-27
A	----- ALIZADEH A ET AL: "THE LYMPHOCHIP: A SPECIALIZED CDNA MICROARRAY FOR THE GENOMIC-SCALE ANALYSIS OF GENE EXPRESSION IN NORMAL AND MALIGNANT LYMPHOCYTES" COLD SPRING HARBOR SYMPOSIA ON QUANTITATIVE BIOLOGY, BIOLOGICAL LABORATORY, COLD SPRING HARBOR, NY, US, vol. 64, no. 1, 1999, pages 71-78, XP001099007 ISSN: 0091-7451 the whole document	1-27
A	----- FRIEDMAN A D: "Leukemogenesis by CBF oncoproteins" LEUKEMIA (BASINGSTOKE), vol. 13, no. 12, December 1999 (1999-12), pages 1932-1942, XP002269493 ISSN: 0887-6924 the whole document	1-27
A	----- DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2001 (2001-11-16), SCHOCH CLAUDIA ET AL: "AML with recurring chromosome abnormalities as defined in the new WHO-classification: Incidence of subgroups, additional genetic abnormalities, FAB subtype and age distribution in an unselected series of 1897 cytogenetically and molecularly analysed AML" XP002269494 Database accession no. PREV200200241183 abstract	1-27
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>& BLOOD, vol. 98, no. 11 Part 1, 16 November 2001 (2001-11-16), pages 457a-458a, 43rd Annual Meeting of the American Society of Hematology, Part 1; Orlando, Florida, USA; December 07-11, 2001 ISSN: 0006-4971</p> <p>-----</p> <p>DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2002 (2002-11-16), KOHLMANN ALEXANDER ET AL: "A Simplified and Partially Automated Target Preparation Method for Gene Expression Profiling." XP002269495 Database accession no. PREV200300367771 abstract & BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 4287, 44th Annual Meeting of the American Society of Hematology; Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971</p> <p>-----</p>	1-27

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Article 52 (2)(d) EPC - Presentation of information (Claims 22-27)

The claims were only searched with regards to the underlying method of generating a reference data base for distinguishing CBF-positive from
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-27 (partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Article 52 (2)(d) EPC - Presentation of information (Claims 22-27)

The claims were only searched with regards to the underlying method of generating a reference data base for distinguishing CBF-positive from CBF-negative AML subtypes.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-27 (partially)

A method for distinguishing CBF-positive AML subtypes, preferably AML_t(8;21) and/or AML_inv(16), from CBF-negative subtypes, preferably from AML_inv(3), AML_7(15;17), AML_MLL, and /or AML_komplex, the method comprising determining the expression level of the marker CKLFSF4. Use of said marker for the manufacture of a diagnostic. A diagnostic kit containing said marker and an apparatus comprising a reference data bank, wherein the reference data bank is obtainable by determining the expression level of CKLFSF4.

2. claims: 1-27 (all partially)

Inventions 2-750

Methods for distinguishing CBF-positive AML subtypes, preferably AML_t(8;21) and/or AML_inv(16), from CBF-negative subtypes, preferably from AML_inv(3), AML_7(15;17), AML_MLL, and /or AML_komplex, and methods for distinguishing specific subtypes against all other AML subtypes and against each other, the method comprising determining individually the expression level of the markers listed in tables 1.1, positions 2-50, tables 1.2-1.5 and in table 2. Use of said markers for the manufacture of diagnostics. Diagnostic kits containing said markers and apparatus' comprising a reference data bank, wherein the reference data bank is obtainable by determining the expression levels of said markers.

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03039443	A	15-05-2003	EP 1308522 A1	07-05-2003
			WO 03039443 A2	15-05-2003
			EP 1470247 A2	27-10-2004

EP 1043676	A	11-10-2000	CA 2304876 A1	09-10-2000
			EP 1043676 A2	11-10-2000
			JP 2001017171 A	23-01-2001
			US 2003017481 A1	23-01-2003
			US 6647341 B1	11-11-2003
			US 2003073083 A1	17-04-2003
